

Breast Cancer Incidence in U.S. Radiologic Technologists

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BACKGROUND. Studies of atomic bomb survivors and medically exposed populations have demonstrated an increased risk of breast cancer associated with acute or protracted, intermediate-dose or high-dose, ionizing radiation; however, the risks associated with low-dose and low-dose-rate (protracted) exposures are less certain.

METHODS. The authors evaluated incident breast cancer risks from 1983 to 1998 according to employment characteristics and a 4-level proxy index for cumulative radiation exposure based on 2 mail surveys among 56,436 U.S. female radiologic technologists who were certified from 1925 to 1980, adjusting for established breast cancer risk factors.

RESULTS. During follow-up, 1050 new breast cancer diagnoses were ascertained. Compared with radiologic technologists who began working in 1970 or later, adjusted breast cancer risks for those who first worked in the 1960s, 1950s, 1940s, from 1935 to 1939, and before 1935 were 1.0 (95% confidence interval [CI], 0.8-1.2), 1.2 (95% CI, 0.9-1.6), 1.0 (95% CI, 0.7-1.5), 1.8 (95% CI, 1.0-3.2), and 2.9 (95% CI, 1.3-6.2), respectively. The risk rose with the number of years worked before 1940 (*P* value for trend = .002) and was elevated significantly among those who began working before age 17 years (relative risk, 2.6; 95% CI, 1.3-5.1; 10 women) but was not related to the total years worked in the 1940s or later. Compared with technologists who had a Level 1 (minimal) proxy index for cumulative radiation exposure, breast cancer risks were 1.0 (95% CI, 0.9-1.2), 1.0 (95% CI, 0.7-1.3), and 1.5 (95% CI, 1.0-2.2), respectively, for technologists who had Level 2, Level 3, and Level 4 (highest) exposure.

CONCLUSIONS. Breast cancer risk was elevated significantly in female radiologic technologists who experienced daily low-dose radiation exposures over several years that potentially resulted in appreciable cumulative exposure. The increased risk for total years worked before 1940, but not later, was consistent with decreasing occupational radiation exposures, improvements in radiation technology, and more stringent radiation protection standards over time. *Cancer* 2006;106:2707-15. © 2006 American Cancer Society.

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Breast cancer is a leading cause of cancer incidence and death among women in the United States¹ and consistently has been linked with acute and fractionated intermediate-dose and high-dose ionizing radiation exposure; the risk from protracted low-dose radiation exposure is less certain.²⁻⁴ Current understanding of the radiation-related breast cancer risk derives primarily from epidemiological studies of the Japanese atomic bomb survivors, who had a single exposure, and medically irradiated patients, who generally received high fractionated exposures over relatively short periods. Of concern

are the repeated low-dose radiation exposures experienced by the general populace from medical procedures, nuclear and medical occupations, air travel, and other sources.^{5,6} Animal studies show lower breast cancer risks for a given dose administered over a longer period than over a short interval, likely because of a greater opportunity for DNA repair, although debate continues about the applicability of these observations to humans.^{5,7,8}

Previous studies of medical radiation workers included few or no women and had limited dose, employment, or other risk factor data.⁹ The few women in the nuclear industry had extremely low radiation exposures.¹⁰ To increase the limited data on incident breast cancer risks associated with chronic low-dose radiation exposure, we report the results from a nationwide cohort study of U.S. radiologic technologists.

MATERIALS AND METHODS

Study Population and Follow-Up

Detailed study and follow-up methods have been described previously.^{11,12} Briefly, the study cohort includes 146,022 (106,953 female) radiologic technologists who were certified by the American Registry of Radiologic Technologists (ARRT) from 1923 to 1980. The 39,069 male technologists were excluded from the breast cancer study. Follow-up is conducted through annual recertification with the ARRT; individuals who fail to renew are linked with national address and mortality data bases. In a first survey during the mid-1980s, we collected employment histories, demographic and lifestyle factors, and reproductive and medical histories from 69,524 of 98,233 known living female technologists (71%) by using a self-administered questionnaire. Nonresponse was greater among technologists who were certified in the earlier years compared with more recent years. During the mid-1990s, again using a self-administered questionnaire, we collected updated employment histories, medical exposures, reproductive histories, and other cancer risk factors from 69,998 of 94,508 known living female technologists (74%). This study was approved by the Institutional Review Boards of the National Cancer Institute and the University of Minnesota.

For the breast cancer incidence analysis, there were 56,436 eligible female radiologic technologists who completed the first survey, had no previous history of breast cancer or chest radiotherapy, and completed the second survey or died before September 1998. Excluded were 584 women with breast cancer, 679 women who received radiotherapy to the chest before the first survey, 4 women with invalid dates, plus 11,821 women who did not complete the second survey or link with mortality records for whom breast

cancer results were unavailable. Responders to the second survey were similar to living nonresponders in terms of the year they started working as a radiologic technologist, the total years worked in all periods, the age at which they began working, apron use when they first worked, and the proxy index for cumulative radiation exposure (data not shown).

Breast Cancer Validation

There were 923 self-reported breast cancers diagnosed between the first and second surveys. Pathology or other medical reports were obtained for 766 of these cancers (83%), and all but 7 (99%) were confirmed as breast cancer (82% confirmed as invasive, and 17% confirmed as *in situ*). We also included 157 self-reported patients with unavailable medical records because of the high positive predictive value and 147 patients who were identified from death certificates, because medical records confirm >98% of breast cancers reported on death certificates in the United States.¹³ In total, 1050 women with breast cancer were studied. Deceased patients were a little older at the first survey (mean age, 48.2 years) than the patients with medically validated cancer (44.4 years) and self-reported cancer (43.6 years). Patients in these groups did not differ in terms of race (95-97% Caucasian).

Demographic, Lifestyle, Medical Radiation, and Established Breast Cancer Risk Factors

Demographic, lifestyle, personal medical radiation, reproductive, breast biopsy (as a surrogate for benign breast disease), and family breast cancer histories were ascertained from the first survey and were updated by using data from the second survey.

Employment Factors and Proxy Index for Cumulative Radiation Exposure

Based on questionnaire data, we categorized women by total years worked as a radiologic technologist, number of years worked in each decade, calendar year began working, age began working, types of procedures performed, and other work practices. We also developed a proxy index for cumulative radiation exposure by combining year began working, total years worked, and work facility (hospital or physician office) data that weight the years worked by calendar period, because radiation exposure decreased substantially over time. We estimated doses for 5 periods (before 1940, from 1940 to 1949, from 1950 to 1959, from 1960 to 1976, and from 1977 to 1984), deriving estimates from the literature on badge and other measurements¹⁴⁻²⁴ for the first 3 periods, and from badge records of cohort members that could be obtained for the latter 2 periods. From a large badge dose survey of

U.S. medical radiation workers from 1960 to 1985, we assigned an average weight of 1.3 for each year worked in a hospital compared with 1.0 for each year worked in a physician's office.²⁵ We summed the weighted proxy exposure estimates from year first worked through 1984 (the start of the first survey). We divided the log-normally distributed cohort exposure estimates into 4 groups (Level 1 [minimal], Level 2, Level 3, and Level 4 [highest]), selecting cut-off values to ensure a wide range in estimated exposure and adequate sample sizes.

Statistical Analyses

Women were followed from completion of the first survey until last follow-up (i.e., the date of reported breast cancer diagnosis, death, or response to the second questionnaire, whichever came first). For breast cancers that were identified from death records, diagnosis dates were imputed by using average age and calendar year survival from population-based registry data.²⁶

Cox proportional hazards regression models were used to compute relative risks (RRs) with 95% confidence intervals (95% CIs)²⁷ with attained age used as the survival time variable²⁸ and stratifying at baseline for 5-year birth cohorts to control for secular trends. Confidence intervals and significance tests were based on the asymptotic, normal distribution of the risk estimates. Except where noted, trend tests were based on the underlying continuous variables. Breast cancer risks were assessed in statistical models with and without adjustment for major risk factors that were related significantly to breast cancer in our cohort and for other, selected work history variables. Because findings were the same whether or not women with in situ breast cancer were included, we present results for invasive and in situ combined.

Missing values were imputed by using 2 different methods: mean values for women of similar age (for menopause and history of breast biopsy) when ages at occurrence were unknown and the nearest-neighbor techniques²⁹ for women who died without completing the second survey. Imputed variables were the number of live births (2.7% of 56,436 women), age at first live birth (3.0%), menopausal status (2.9%), age at menopause (5.7%), oral contraceptive use (2.0%), hormone replacement therapy use (2.6%), age first used hormone replacement therapy (4.0%), family history of breast cancer (7.5%), personal history of breast biopsy (3.1%), and age at first breast biopsy (3.5%). Analyses were conducted with and without imputed values. Analyses in which imputed values were used yielded negligibly different risk estimates compared

with analyses in which the missing values were included in separate, unknown categories.

RESULTS

On average, women with breast cancer and women in the comparison group worked as radiologic technologists for 13.8 years and 11.1 years, respectively, and were similar in terms of education, race, marital status, and geographic region of residence (Table 1). Women with breast cancer began working as radiologic technologists an average of 6 or 7 years before other female technologists, did not differ in certification specialty, and were only slightly older when they began working (mean ages, 21.2 years and 20.5 years).

Breast cancer risk increased significantly with attained age (P trend < .0001), and risks according to reproductive and other factors generally were as expected (see Table 2). Risk increased with increasing height (P trend = .0005) but was not related to the number of alcoholic drinks consumed per week; pack-years of cigarette smoking; body mass index; the number of personal diagnostic X-ray procedures (e.g., angiography, upper gastrointestinal series); conventional X-rays to the head, neck, or trunk; any diagnostic or therapeutic radioisotope procedures; or any external beam radiotherapy (recall that women were excluded from the study if they had received prior radiotherapy to the chest) (data not shown).

In analyses that were adjusted for major breast cancer risk factors and for other, selected work history variables (see Table 3, footnotes), radiologic technologists who began working before 1940 had a 2-fold statistically significant elevated risk of breast cancer, and technologists who began working before 1935 ($n = 15$ women) had a nearly 3-fold significantly elevated risk compared with technologists who began working in 1970 or later. Risks were not elevated in technologists who began working in the 1940s, 1950s, or 1960s. The breast cancer risk increased significantly with increasing number of years worked before 1940, but it was not associated with the number of years worked in the decades after 1940 or with the total number of years worked as a radiologic technologist. The breast cancer risk was elevated significantly among those who began working before age 17 years (RR, 2.6; 95% CI, 1.3-5.1), based on 10 individuals, and rose with decreasing age at which women began working as radiologic technologists (P trend = .05). The risk was elevated from 10% to 30% among women in all but the highest category of the number of times technologists held patients for X-ray procedures, but it was not associated with the number of times technologists underwent practice X-rays. Apron or shield use when first working was not associated with decreased risk

TABLE 1
Characteristics of the Breast Cancer Group and a Female Comparison Group: U.S. Radiologic Technologists Study

Characteristic*	Cohort Person-Years	Breast Cancer Group (N = 1050)	Comparison Group (N = 55,386)
Education†			
High school or less	2494	1.0	0.5
Vocational	12,664	2.7	2.2
Radiation technology program	349,403	58.7	60.0
Some college or graduate school	197,759	34.7	34.3
Other	14,134	2.2	2.5
Race			
White	560,640	96.4	96.6
Black	11,336	2.1	2.0
Asian/Pacific Islander	3549	0.8	0.6
American Indian/Alaska Native	1043	0.3	0.2
Other or unknown	3434	0.5	0.6
Marital status			
Currently married	435,259	71.2	74.8
Divorced or separated	58,267	11.7	10.2
Widowed	10,706	4.3	2.0
Never married	70,246	11.6	12.1
Geographic region of residence‡			
South	141,432	24.0	24.5
Northeast	150,338	24.8	25.9
Midwest	189,451	30.8	32.5
West	98,682	20.5	17.1
Year of birth§		(1940)	(1947)
<1930	34,579	18.1	6.4
1930–1939	70,500	24.1	12.2
1940–1949	188,366	39.1	32.2
1950–1959	280,716	18.7	48.2
≥1960	5841	0.0	1.0
Age at first survey, y		(44.8)	(37.4)
<30	128,512	5.3	21.3
30–39	269,181	31.7	46.4
40–49	119,426	33.3	20.8
50–59	42,594	17.2	7.5
≥60	20,289	12.4	4.0
Certification specialty			
Radiology	541,016	93.5	93.3
Radiation therapy	2736	0.3	0.5
Nuclear medicine	9037	1.5	1.6
Combination	27,213	4.7	4.7

* Characteristics reflect status as of response to the first (baseline) survey. Percentages may not sum to 100, because data are not shown for individuals with unknown values.

† Individuals were placed in the "highest" educational category applicable, with college ranked after radiological technology training, which ranked after high school education.

‡ Based on U.S. Census Bureau definitions for geographic regions.

§ Numbers in parentheses are mean values.

overall; however, the risk was 10% to 20% lower for technologists who began working before 1950.

Most radiologic technologists performed multiple procedures (including fluoroscopy and multifilm and routine diagnostic X-rays), and breast cancer risks according to the years these procedures initially were performed were similar to the risks for the years the women began working as radiologic technologists (data not shown). Risks were not associated with the years women began working with therapeutic X-rays

or nuclear medicine procedures or with the number of years women performed any of 14 individual procedures (i.e., intravenous pyelogram, barium enema, Cobalt 60).

Technologists in the Level 4 (highest) proxy cumulative radiation exposure category had a statistically significant 50% greater risk compared with technologists in the Level 1 (minimal) exposure category (Table 3). The risks for technologists in the Level 2 and Level 3 exposure categories did not differ from unity.

TABLE 2
Adjusted Relative Risks for Breast Cancer Incidence Among Female Radiologic Technologists According to Reproductive and Other Risk Factors

Risk Factor	No. of Breast Cancer Patients	RR*	95% CI
Age at menarche, y			
≥15	93	1.0	—
13–14	453	1.1	0.9–1.4
11–12	409	1.1	0.9–1.4
<11	65	1.2	0.9–1.6
<i>P</i> trend†		(.71)	
No. of live births			
0	277	1.0	—
1–2	468	0.7	0.6–0.9
3–4	234	0.7	0.6–0.8
≥5	30	0.6	0.4–0.8
<i>P</i> trend†		(.0005)	
Age at first live birth, y			
<25	335	1.0	—
25–29	305	1.2	1.1–1.5
30–34	102	1.2	1.0–1.6
35–39	23	0.9	0.6–1.5
≥40	8	2.0	1.0–4.0
<i>P</i> trend†		.02	
Menopause status			
Premenopausal	379	1.0	—
Postmenopausal	671	1.4	1.1–1.7
Age at menopause, y			
<40	188	1.0	—
40–44	110	1.4	1.1–1.8
45–49	203	1.6	1.3–2.1
≥50	170	1.4	1.1–1.8
<i>P</i> trend†		<.0001	
Family history of breast cancer			
No	581	1.0	—
Yes	469	1.4	1.2–1.6
Personal history of breast biopsy†			
No	706	1.0	—
Yes	344	1.8	1.5–2.2
Age at first breast biopsy, y			
<40	166	1.0	—
40–49	109	1.0	0.8–1.3
50–59	40	1.1	0.8–1.6
≥60	29	2.8	1.8–4.3
<i>P</i> trend†		<.0001	
Oral contraceptive use			
No	357	1.0	—
Yes	693	1.0	0.9–1.2
Hormone-replacement therapy			
No	672	1.0	—
Yes	378	0.8	0.7–1.0

RR: relative risk; 95% CI: 95% confidence interval.

* Relative risks were estimated from a single Cox proportional hazards multiple regression model that included all the variables listed in Table 2, plus the number of alcoholic drinks consumed per week (<1, 1–6, 7–13, or ≥14), the number of cigarette pack-years smoked (0, 1–9, 10–19, 20–29, 30–39, or ≥40), height (<160 cm, 160–164 cm, 165–169 cm, 170–174 cm, or ≥175 cm), and body mass index (<18.5 kg/m², 18.5–24.9 kg/m², 25.0–29.9 kg/m², 30.0–39.9 kg/m², or ≥40 kg/m²). The model was adjusted for age (time scale) and was stratified on birth cohort in 5-year intervals. Age at first live birth, the number of live births, menopausal status, age at menopause, personal history of breast biopsy, age at first breast biopsy, and hormone-replacement therapy were treated as time-dependent variables. Risk estimates are not shown for unknown categories.

† Trend tests were based on the slope estimate of the underlying continuous variable; parentheses indicate a negative slope estimate.

‡ Breast biopsies were counted only if they occurred at least 1 year before a breast cancer diagnosis.

DISCUSSION

The U.S. Radiologic Technologists (USRT) cohort is the largest group of female medical radiation workers ($n = 56,436$ women) with low-dose-rate exposures studied to date. Based on 1050 incident breast cancers, breast cancer incidence risk was elevated significantly in women who experienced daily small radiation exposures that cumulated over several years to potentially high levels compared with women who had minimal cumulative exposures. We also observed significant (2-fold to 3-fold) breast cancer risks among women who began working before 1940 (vs. 1970 or later) or at ages younger than 17 years (vs. 30 years or older), and there was significantly increasing risk with increasing number of years worked before 1940. Adjustment for established breast cancer risk factors had minimal effect on the radiation-related breast cancer risk estimates. Results from the current study provided no evidence of an elevated risk for technologists who began working in the 1940s or later, technologists who worked for several decades, or technologists who began working at age 17 years or older.

Only 2 substantially smaller studies of female medical radiation workers have provided estimates of breast cancer risk. Among 27,000 (20% female) Chinese diagnostic X-ray workers, women who were exposed before 1950 and from 1950 to 1985 had 70% and 50% greater breast cancer incidence risks, respectively, compared with other female medical workers who were not exposed to radiation³⁰; however risk was not elevated among women who worked in later periods.³¹ Those findings parallel the current results, because occupational radiation exposures likely were greater among Chinese medical radiation workers than among U.S. medical radiation workers during the same periods.³² In contrast, 4200 (82% female) Danish radiotherapy workers who were employed from 1954 to 1982 experienced breast cancer incidence similar to that among Danish women in the general population, and the risk was not related to the measured radiation dose (cumulative from 1954 onward) or to the total years of exposure.³³

Overall, incident breast cancer risk was not greater for 101,164 Canadian female radiation workers who were monitored during 1951 to 1983 compared with Canadian women in the general population, although findings were not described separately for the 35% of women who were medical radiation workers, and dose-response results were not reported for breast cancer.³⁴ Unfortunately, the absence of meaningful numbers of female nuclear workers¹⁰ prevents a comparison of breast cancer risk between the USRT cohort

TABLE 3
Relative Risks for Breast Cancer Incidence Among Female Radiologic Technologists According to Employment Characteristics and a Proxy Index for Cumulative Radiation Exposure

Characteristic	Cohort Person Years	No. of Breast Cancer Patients	Unadjusted*		Adjusted ^{†‡}	
			RR	95% CI	RR	95% CI
Year began working as a radiologic technologist						
≥1970	286,608	225	1.0	—	1.0	—
1960–1969	181,433	371	1.0	0.8–1.2	1.0	0.8–1.2
1950–1959	74,115	284	1.2	0.9–1.6	1.2	0.9–1.6
1940–1949	20,920	101	1.1	0.7–1.6	1.0	0.7–1.5
<1940	4694	40	2.1	1.2–3.6	2.0	1.1–3.4
1935–1939	2920	26	1.9	1.1–3.4	1.8	1.0–3.2
<1935	1774	14	3.1	1.4–6.7	2.9	1.3–6.2
<i>P</i> trend [‡]			(.05)		(.06)	
Total no. of years worked						
<10	292,846	404	1.0	—	1.0	—
10–19	219,256	383	0.9	0.8–1.1	0.9	0.8–1.0
20–29	44,837	176	1.1	0.9–1.4	1.1	0.9–1.3
≥30	10,830	58	1.1	0.8–1.5	0.9	0.7–1.3
<i>P</i> trend			.33		.97	
No. of years worked before 1940						
0	16,361	89	1.0	—	1.0	—
1–4	2850	26	1.9	1.2–3.1	1.9	1.1–3.3
≥5	1843	14	2.5	1.3–4.9	2.5	1.2–5.1
<i>P</i> trend			.001		.002	
No. of years worked during 1940–1949						
0	40,937	182	1.0	—	1.0	—
1–4	16,243	82	1.0	0.7–1.3	0.9	0.7–1.3
≥5	9049	56	1.1	0.7–1.5	0.9	0.6–1.4
<i>P</i> trend			.50		.66	
No. of years worked during 1950–1959						
0	95,178	264	1.0	—	1.0	—
1–4	59,635	220	1.1	0.8–1.3	1.1	0.9–1.4
≥5	35,779	175	1.1	0.9–1.4	1.1	0.9–1.4
<i>P</i> trend			.47		.66	
No. of years worked during 1960 or later						
0	17,506	81	1.0	—	1.0	—
1–4	83,732	150	1.1	0.8–1.5	1.1	0.8–1.5
≥5	466,530	790	1.0	0.8–1.3	1.0	0.8–1.3
<i>P</i> trend			.67		.81	
Age began working, y						
≥30	20,553	71	1.0	—	1.0	—
25–29	26,817	76	1.2	0.9–1.7	1.2	0.8–1.6
20–24	252,319	404	1.2	0.9–1.6	1.1	0.9–1.5
17–19	266,050	460	1.3	1.0–1.7	1.2	0.9–1.6
<17	2030	10	2.7	1.4–5.3	2.6	1.3–5.1
<i>P</i> trend			(.03)		(.05)	
No. of times held patients for X-rays						
0	22,652	42	1.0	—	1.0	—
1–9	60,267	117	1.2	0.8–1.7	1.2	0.8–1.7
10–24	90,133	176	1.3	0.9–1.8	1.3	0.9–1.8
25–49	105,909	188	1.2	0.8–1.6	1.1	0.8–1.6
≥50	291,339	497	1.0	0.7–1.4	1.0	0.7–1.4
<i>P</i> trend [§]			(.09)		(.07)	
No. of times allowed others to take practice X-rays						
0	520,842	899	1.0	—	1.0	—
1–9	40,086	101	1.	0.8–1.3	1.0	0.8–1.3
10–24	7780	22	0.9	0.6–1.3	0.8	0.5–1.3
≥25	2537	11	1.2	0.7–2.3	1.2	0.7–2.3
<i>P</i> trend [§]			.87		.96	
Used lead apron when began working (all periods)						
No	546,299	955	1.0	—	1.0	—
Yes	21,871	64	1.1	0.8–1.4	1.1	0.8–1.4
Used lead apron when began working before 1940						
No	1348	13	1.0	—	1.0	—
Yes	3103	25	0.9	0.4–1.7	0.8	0.4–1.6

(continued)

TABLE 3
(continued)

Characteristic	Cohort Person Years	No. of Women	Unadjusted*		Adjusted ^{††}	
			RR	95% CI	RR	95% CI
Used lead apron when began working during 1940–1949						
No	3855	21	1.0	—	1.0	—
Yes	16,537	73	0.8	0.5–1.3	0.9	0.5–1.4
Proxy index for cumulative radiation exposure						
Level 1 (minimal)	441,458	549	1.0	—	1.0	—
Level 2	109,023	344	1.1	0.9–1.3	1.0	0.9–1.2
Level 3	22,756	105	1.1	0.8–1.4	1.0	0.7–1.3
Level 4 (maximal)	6765	52	1.7	1.1–2.5	1.5	1.0–2.2
P trend [§]			.03		.11	

RR: relative risk; 95% CI: 95% confidence interval.

* Relative risks were estimated by using Cox proportional hazards regression analysis. Unless otherwise stated, the timeline was attained age, and all analyses were stratified on birth cohort in 5-year intervals. Risk estimates are not shown for unknown categories, although “unknown” was a category that was included in the models. The year first worked was adjusted for total years worked, and vice versa. The number of years worked in each period was limited to the subset of individuals who were eligible to work (i.e., ≥ 14 years of age) during the period and was adjusted for the number of years worked in all other periods. The number of times patients were held for X-ray, the use of protective apron or shield when first worked, and the number of times others were allowed to take practice X-rays during training were adjusted for the year first worked. Analyses for years worked in different periods were restricted to women who were eligible to work in those periods (i.e., age ≥ 14 years).

[†] Breast cancer risk factors that were included in all models were family history of breast cancer (no/yes), age at menopause (<40 years, 40–44 years, 45–49 years, ≥ 50 years, or premenopausal), number of live births (0, 1–4, or ≥ 5), age at first live birth (<25 years, 25–29 years, or ≥ 30 years), and age at first breast biopsy (<60 years, ≥ 60 years, or no biopsy). Age at menopause, age at first live birth, number of live births, and age at first breast biopsy were included as time-dependent variables. Breast biopsies were counted only if they occurred at least 1 year before a breast cancer diagnosis.

^{††} Unless otherwise stated, trend tests were based on the slope estimate of the underlying continuous variable (parentheses indicate a negative slope estimate).

[§] Trend tests were based on the slope estimate of the category scores. For the number of times others were allowed to take practice X-rays and for the proxy index for cumulative radiation exposure, the categories were 0, 1, 2, 3; for the number of times patients were held for X-rays, the categories were 0, 1, 2, 3, and 4.

and the nuclear workers, who also had chronic low-dose exposures.

The elevated breast cancer risk among radiologic technologists with the highest level proxy index for cumulative radiation exposure agrees with substantial excesses in patients with tuberculosis, who received multiple fluoroscopies over years and cumulated an average of 0.5–1.0 gray (Gy),^{7,35} and they also are consistent with the substantially greater occupational radiation exposures early in the 20th century. The reduction in the recommended exposure limits, from an annual level of 3 Sv in 1902 to 0.7 Sv in the mid-1920s, to 0.3 Sv in 1934, to 0.15 Sv in 1949, to 0.05 Sv in 1957, and to the current 5-year annual average of 0.02 Sv (not to exceed 0.05 Sv in any single year) in 1990,^{36–38} paralleled the introduction of new radiation technologies that improved image quality while substantially reducing patient and staff exposures.³⁹ Based on measurements in the scientific literature, we conclude that average doses for hospital workers were high before 1940 (≈ 100 mSv per year) and dropped substantially in the 1940s (to ≈ 25 mSv per year).^{14–18}

The elevated risk among technologists who began working at ages younger than 17 years agrees with findings from the A-bomb survivors and from other studies that reported decreasing risk with increasing age at exposure.^{2,4} The most plausible explanation,

i.e., increased sensitivity of breast tissue to radiation carcinogenesis at younger ages, conflicts with stronger increased risks for working before 1940 among technologists who began working at age 20 years and older compared with younger workers (data not shown). In addition, the effect is not caused by confounding through a correlation between the year women began working and the age at which they began working ($r = 0.008$), which renders this finding difficult to interpret. The modestly lower breast cancer risks for women who reported apron or shield use when they began working before 1950 suggests a radiation-related effect. Similarly, modest elevations in the risk observed for women who reported all but the highest category of the number of times patients were held for X-rays, in which the confidence interval was wide (RR, 1.0; 95% CI, 0.7–1.4), are consistent with an association with radiation.

Previously, we reported a significantly greater than expected overall breast cancer incidence rate compared with women in the general U.S. population¹² and statistically significant 2-fold and 3-fold excess mortality risks, although that expectation was based on 255 patients who died of breast cancer, for women who began working during the 1940s and before 1940, increasing risk with increasing number of years worked before 1950 (P trend = .02), and increas-

ing risks with decreasing years that women first performed various diagnostic X-ray procedures.⁴⁰ The risk of dying from breast cancer was from 40% to 60% greater among technologists who began working at ages younger than 25 years (vs. ages 25 years and older), but the risk was not related to the year women first used therapeutic radioisotopes, the number of years they worked with any radiologic procedure, the use of lead aprons, or whether they held patients for X-rays. The main differences between the current incidence study and our earlier mortality study were that breast cancer incidence was elevated significantly only among women who began working before 1940 (vs. before 1950 in the mortality study) and in women who began working at ages younger than 17 years (vs. ages younger than age 25 years in the mortality study). The consistently lower breast cancer incidence and mortality risks among women who began working in more recent calendar years argue against potential confounding in the mortality findings from more recent adjuvant therapy use, leading to improved survival.

Although the proxy index allowed us to semiquantify breast cancer incidence risks, the absence of breast tissue doses for individual technologists remains the major limitation. The association between the proxy index for cumulative radiation exposure and breast cancer may have been attenuated by nondifferential exposure misclassification. Other limitations include the lack of detailed work history information for some cohort members and the restriction of the study population to survivors who completed the mid-1980s questionnaire. On the positive side, mortality follow-up has been comprehensive, and mortality analyses have yielded radiation-related risk estimates consistent with this breast cancer incidence analysis, suggesting that survival bias is limited. The extensive breast cancer risk factor data demonstrated associations consistent with other studies,⁴¹ enhancing the credibility of the findings, and allowed for time-dependent adjustment of covariates. The current study covered a working period of 80 years (1926-2005), a long interval that spanned a wide range of recommended exposure limits and that represented a substantial dose range. Nevertheless, in the absence of individual breast tissue doses, our results need to be interpreted with caution.

We note several public health implications of our findings. With the possible exception of technologists who began working before age 17 years, we found no evidence that more recent radiation dose levels increase breast cancer risk; however, the possibility of elevated cancer risks from fluoroscopically guided diagnostic and interventional procedures is

of growing concern.⁴²⁻⁴⁵ Medical radiation workers and their employers should be cognizant of atypical radiation exposures and should take precautions to minimize them. Workers also should inform their health care providers about their occupational exposure. Because women who worked during the first several decades of the 20th Century may have experienced substantially higher radiation exposures than recommended during more recent decades, they may be at greater risk of radiation-related tumors. Others who work with more recent high-dose procedures also should be monitored. Finally, the cumulative body of data on radiation-related cancer risks suggests that no radiation dose is completely safe at any age⁴⁶; therefore, all radiation workers need to be protected regardless of estimated cumulative dose, and continued epidemiological follow-up is warranted for all USRT members.

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